UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,175	04/19/2006	Graeme Bilbe	33440-US-PCT	7229

1095 7590 02/19/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
JAVANMARD, SAHAR	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
02/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,175	BILBE, GRAEME	
	Examiner	Art Unit	
	SAHAR JAVANMARD	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

This Office Action is in response to Applicant's Restriction Requirement remarks filed on September 19, 2008. Claim(s) 2-8 are pending.

Response to Arguments

In view of Applicant's amendments, the 112 1st rejection of claims 1-7 with regard to "prevention" has been fully considered. The rejection is hereby withdrawn.

In view of Applicant's amendments with respect to the 102(b) rejection of claims 1 and 5-7 as being anticipated by Netzer has been fully considered. The rejection is hereby withdrawn.

Upon further consideration, the following new rejections are being made as set forth in the office action below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d

2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is Shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-4 and 8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 11 of U.S. Patent No. 7,169,791 B2 to Breitenstein et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of treating neurological and vascular diseases using compounds of formula I, whereas the patented claims teach a method of treating leukemias comprising administering the greatly overlapping scope of compounds of formula I. Leukemia is a type of vascular disorder, thus the claims are not patentably distinct over US Patent 7,169,791 B2.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8 rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for the generation of beta-amyloid, does not reasonably provide enablement for the treatment of all neurological and vascular disorders related to beta-amyloid generation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all neurological and vascular disorders are treatable by the generation of beta-amyloid as described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of the treatment of all neurological and vascular disorders related to beta-amyloid generation. The nature of the invention is complex in that it encompases the treatment of all types of neurological and vascular disorders.

(2).Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of neurological and vascular disorders by the compounds of formula I.

(3).Guidance of the Specification:

There is no guidance in the specification as to how one would treatment any neurological and vascular disorder. Guidance is geared toward beta amyloid generation or lack thereof.

(4).Working Examples:

Applicant provides in vitro examples of the cytotoxicity of 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide and its activities in cell-free enzyme assays.

(5).State of the Art.

While the state of the art is relatively high with regard to treating specific disease such as Alzheimer's disease or Down's syndrome, however the state of the art is very low in treating all neurological and vascular disorders related to beta-amyloid generation.

(6).Predictability of the Art.

The invention is directed to the treatment of all neurological and vascular disorders related to beta-amyloid generation. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970).

(7).The Quantity of Experimentation Necessary.

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for the treatment of all neurological and vascular disorders related to beta-amyloid generation. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of all

neurological and vascular disorders with any compound of formula I, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of all neurological and vascular disorders related to beta-amyloid generation with any compound of formula I, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of disorder because there is no known drug effective for the treating all types of neurological and vascular disorders related to beta-amyloid generation. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to the treat all neurological and vascular disorders related to beta-amyloid generation by administration of one of the compounds of formula I within the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for the treatment of all neurological and vascular disorders related to beta-amyloid generation by administering the compounds of formula I of the claims is not considered to be enabled by the instant specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for some compounds encompassed by formula I, namely, 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide, does not reasonably provide enablement for the treatment of all neurological and vascular disorders related to beta-amyloid generation with all the compounds encompassed by formula I as set forth in the instant claims. The specification does not provide sufficient information that all the compounds encompassed by formula I are capable of treating all neurological and vascular disorders related to beta-amyloid generation. Thus, the number of compounds encompassed by formula I are very broad as cited in claims 2-8.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that all the compounds encompassed by formula I are capable of treating all neurological and vascular disorders related to beta-amyloid generation.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is

directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of treating all neurological and vascular disorders related to beta-amyloid generation with the administration of a compound of formula I as described in claims 2-8.

The nature of the invention is complex in that it encompasses the treatment said ailments using a wide array of compounds encompassed by formula I.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass methods of treating all neurological and vascular disorders related to beta-amyloid generation by administering by a wide array of compounds encompassed the formula I. There are countless possible

compounds encompassed by formula I for the treatments claimed. The claims are therefore much broader than the enabling disclosure.

(3). Guidance of the Specification:

The guidance given by the specification as to how effective the disclosed compounds of formula I are at treating the desired ailments is limited, in particular only data for 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide is provided.

(4). Working Examples:

As mentioned above, only examples of how 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide is able to alter beta amyloid secretion is disclosed.

(5). State of the Art:

The state of the art regarding the compounds of formula I is very low. The state of the art regarding any compound capable of treating all neurological and vascular disorders related to beta-amyloid generation is non-existent.

(6). Nature and predictability of the invention

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that “the scope of enablement varies

inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound as encompassed by formula I, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for treating all neurological and vascular disorders related to beta-amyloid generation. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of all neurological and vascular disorders related to beta-amyloid generation with any compound of formula I, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat all neurological and vascular disorders related to beta-amyloid generation by administration of all the compounds encompassed by formula I as set forth in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, methods of treating all neurological and vascular disorders related to beta-amyloid generation by administering the multitude of compounds of formula I of the claims is not considered to be enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 3 5 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "inhibitor" according to claim 2. There is insufficient antecedent basis for this limitation in the claim. In the amendment, “inhibitor” was deleted and was not incorporated in the modification of claim 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Netzer et al. (WO 03/057165 A2).

Netzer teaches methods and compositions for treating amyloid-β-related disorder such as Alzheimer's disease via administration of compounds that modulate, e.g. inhibit, ATP-dependent enzymatic activity such as γ-secretase activity (page 3, lines 28-31). In an embodiment, the enzyme activity is a kinase activity. The compound binds a kinase enzyme exhibiting an ATP-dependent enzymatic activity. In a specific embodiment the kinase is a tyrosine kinase namely, Abl kinase, BCR-Abl kinase, ARG kinase, src kinase,

c-kit, platelet-derived growth factor receptor (PDGFR) (page 43, lines 4-11; claims 1, 33, 37, 38, 102, 103).

Netzer teaches that a treatment regimen can be administered to an elderly person, e.g., age 65 or older. The composition is administered daily with doses ranging from 10μg/day to a maximum of 800μg/day (page 64, lines 10-20), meeting the limitations of claim 5.

Though Netzer does not specifically teach the elected compound 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide, it is encompassed by the formula of figure 1 in claim 79. Specifically the compound is taught when R_1=H; R_2=heteroaryl; R_3=H; R_4=$(C=O)_rO_s(C_1\text{-}C_{10})$alkyl wherein r and s are 0; R_5=$(C=O)_rO_s$heteroaryl wherein r=1 and s=0.

Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to have employed the elected compound 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide as a method of treating a neurological disease that is related to beta amyloid production, namely Alzheimer's disease. The motivation provided by Netzer teaches that the compound 4-methyl-N-[3-(4-methyl-imidazol-1-yl)-5-trifluoromethyl-phenyl]-3-(4-pyridin-3-yl-pyrimidin-2-ylamino)-benzamide is encompassed by the formula of figure 1 and these comupounds are taught by Netzer as being useful in the treatment of Alzheimer's disease.

Conclusion

Claims 2-8 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sahar Javanmard whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/S. J./

Examiner, Art Unit 1617

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617